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6. AUTHOR(S)
Dr. Judy S. Riffle

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Virginia Tech Dept. of Chemistry (0212) Blacksburg, VA 24061	4-30971

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AFOSR, Attn: Hugh DeLong, Program Manager Biomimetics, Biomaterials and Biointerfacial Sciences Directorate of Chemistry and Life Sciences 801 N. Randolph St., Arlington, VA 22203-1977 1954 4015 Wilson Blvd Room 715	F49620-02-1-0308

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13. ABSTRACT (Maximum 200 Words)
Complexes of magnetic nanoparticles with polymer dispersion stabilizers can lead to well-defined magnetic dispersions and also to precursors for magnetic microspheres. Thus, complexes of block copolymers containing both hydrophilic and hydrophobic dispersion components with magnetite nanoparticles have been prepared and characterized. In-vitro cell survival assays of the hydrophilic complexes suggest a relationship between cell survival and proliferation and the molecular weight (and hydrophilicity) of the polymer dispersants (higher molecular weight results in better cell proliferation/survival). Magnetic transition metals such as cobalt, iron or nickel are susceptible to oxidation with concurrent loss in magnetic response unless the nanoparticle surfaces are protected with oxygen impermeable coatings. Copolymer precursors to graphitic-like and silica-like protective coatings have been prepared and utilized to coat cobalt nanoparticles in thermolysis reactions. High temperature pyrolyses of the complexes in both cases suggest that oxidatively stable cobalt nanoparticles approximately 10 nm in diameter can be formed. The pyrolysis procedure results in 10-nm cobalt but the particles are adhered together. Attention will be devoted during the forthcoming year on methods for separating the nanoparticles from each other and on "re-coating" the materials with appropriate biospecific functional groups.

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Program Title: SEEDLING Proposal to Establish Pilot Data for a Consortium on Magnetic Nanoparticle Assemblies: A New Tool for Drug Delivery, Sensors and Electronic Devices

Sponsor # F49620-02-1-0308

Submitted by:
    Prof. Judy Riffle, Principal Investigator
    Department of Chemistry (0212)
    Virginia Tech
    Blacksburg, VA 24061

A. **Personnel Supported:**
   - Victor Baranauskas, PhD Candidate, Macromolecular Science and Engineering Program
   - Anita Carmichael, PhD Candidate, Macromolecular Svience and Engineering Program
   - Michael (Shane) Thompson, PhD Candidate, Dept. of Chemistry
   - Michael Zalich, PhD Candidate, Dept. of Chemistry

B. **Publications During the Reporting Period:**
   L. A. Harris, J. D. Goff, A. Y. Carmichael, J. S. Riffle, J. J. Harburn, T. G. St. Pierre and M. Saunders, "Magnetite Nanoparticle Dispersions Stabilized with Triblock Copolymers," Chemistry of Materials, 15(6), 1367-1377 (2003).

   Publications in Progress:
   M. L. Vadala, M. Rutnakornpituk, A. R. Esker and J. S. Riffle, "Block Copolysiloxanes and their Complexation with Cobalt Nanoparticles," submitted to Polymer, 2003.

   Sheng Lin-Gibson,* Vivek M. Prabhu, and Charles C. Han, "Morphological Characterization of Micellar Structures in Triblock Siloxane Copolymer Solutions," submitted to Polymer, 2003.

C. **Invention Disclosures and Patents Granted: n/a**

D. **Invited Lectures, Presentations, Talks, etc.:**

   1. Judy Riffle, Virginia Tech, and J. P. Dailey, Case Western Reserve University "Controlled Nanomagnetic Biomaterials for Ophthalmic Applications," invited lecture presented at Polymers in Medicine and Biology: 2002, November 13-16, 2002.

2. Judy Riffle, "Controlled Macromolecular-Magnetic Particle Complexes and Dispersions," presented at Appalachian State University, October, 2002.
3. Judy Riffle, "Complexes of Polymers with Magnetic Nanoparticles for Biomedical Applications," presented at Roanoke College, November, 2002.
4. Judy Riffle, "Synthesis of Magnetic Nanoparticles," presented at University of South Carolina at Spartanburg, March, 2003.
5. Judy Riffle, "Magnetic Nanoparticle Assemblies: A New Tool for Drug Delivery, Sensors, and Electronic Devices," presented at the DARPA BioMagnetICs Kickoff Meeting, San Diego, CA, July 9-11, 2003.
6. J.S. Riffle, K.W. O'Brien, U.O. Hafeli, J.P. Dailey and D. Bardenstein, "Macromolecule-magnetic nanoparticle complexes for ocular therapies," presented at 5th International Symposium on Frontiers in Biomedical Polymers, Ischia Island, Italy, September 10-13, 2003.

Research Findings During the Reporting Period:

Cobalt Nanoparticles Coated with Thin Protective Layers to Avoid Cobalt Oxidation

Oku et al. have reported preparing carbon nanocapsules containing SiC and Au nanoparticles by heating poly(vinyl alcohol)-nanoparticle complexes under argon at 500 °C [1]. Their findings support our working hypothesis that controlled pyrolyses of magnetic transition metal-polymer complexes in inert atmospheres could provide a method for forming metal nanoparticles coated with a protective, highly carbonaceous or silaceous residue. This is important since uncoated or polymer-coated transition metal particles such as cobalt, nickel or iron are susceptible to oxidation with concurrent loss in magnetic properties. It is also reasonable that our approach of utilizing metal carbonyls to generate metal nanoparticles in the presence of block copolymer dispersion stabilizers, followed by thermolysis of the complexes to form protective shells should be significantly easier to scale relative to alternative arc-discharge methods. It is hoped that the protected metal nanoparticles can be ground to fine powders with a combination of high-energy milling and ultra-sonication, then appropriately functionalized for dispersion in aqueous media. Durability investigations, methods for obtaining fine powders, and their subsequent functionalization will be the major focus of synthetic efforts over the next year. Our collaboration with Prof. St. Pierre's biophysics research group in Australia will be valuable for understanding magnetic properties of these materials, and for understanding relationships between the durability of magnetic response in air and water and any evolution of magnetic properties.

Figure 1. Diblock copolymers for templating small diameter cobalt nanoparticles. For the polysiloxane copolymers, these will be designated PDMS-*b*-[PVMS-*co*-PMTES] for those containing ethoxysilyl pendent groups and PDMS-*b*-[PMVS-*co*-PMTMS] for polymers with methoxysilyl pendent groups.

Over the past year, we have designed and demonstrated syntheses of block copolymers based on both silicon and carbon (figure 1) which (1) can be utilized to avoid aggregation during formation of ≈10-15 nm diameter cobalt and (2) the polymers form stable residues upon heating at 600-700 °C. Our approach has built upon recent years work. Dicobalt octacarbonyl has been thermolyzed in the presence of toluene solutions of these block copolymers to form cobalt nanoparticles. Subsequent heat-treatments of the cobalt particle-polymer complexes have been investigated in efforts to form protective carbonaceous or silaceous coatings on the cobalt surfaces. The primary objectives of this years research described in this section have included (1) preparing cobalt nanoparticles of a sufficiently small size that aggregation could be avoided by utilizing the
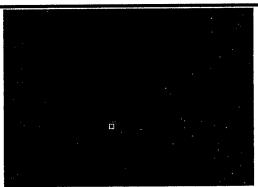

Figure 2. Cobalt nanoparticles encapsulated in a poly(styrene-*b*-vinylphenoxyphthalonitrile) copolymer. The vinylphenoxyphthalonitrile block anchors to the cobalt surface and the polystyrene block extends into the toluene reaction solvent to keep the particles from aggregating.

block copolymer dispersion stabilizers, (2) forming thin, protective sheaths on the particle surfaces to inhibit oxygen ingression and retain high magnetic susceptibility over time, and (3) retaining the cobalt particle size during the elevated temperature step in which the protective overlayers were formed.

Styrenic block copolymers (top of figure 1) were prepared by sequential living anionic copolymerization of styrene, then 4-*t*-butyldimethylsiloxystyrene at –78 °C in THF. The *t*-butyldimethylsilyl protecting group were removed with acid, then the pendent phenols were derivatized with 4-nitrophthalonitrile in base (nucleophilic aromatic substitution). The polysiloxane depicted at the bottom of figure 1 was prepared by sequential living anionic polymerization of hexamethylcyclotrisiloxane followed by 1,3,5-trimethyl-1,3,5-trivinylcyclotrisiloxane in cyclohexane/THF at room temperature. Portions of the pendent vinyl groups were then hydrosilated with either triethoxysilane or trimethoxysilane utilizing Pt^0 as the catalyst. Thus far, the best degree of hydrosilation for forming stable cobalt nanoparticle dispersions has been to functionalize 50% of the repeat units in the anchor block. The sequences of these copolymers in the anchor block are assumed to be random.
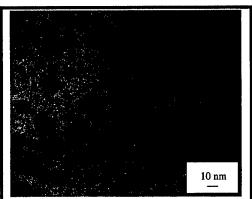

Figure 3. Cobalt nanoparticles coated with a 16,000 g mol^{-1} PDMS-3900 g mol^{-1} PMVS-co-PMTMS copolymer. The PMTMS block anchors to the cobalt surface and the PDMS tail block provides dispersion stability in the toluene reaction solvent.

Both our work [2-4] and the work of others [5,6] have demonstrated that 10-15 nm diameter cobalt particles can be prepared by thermolyzing dicobalt octacarbonyl in the presence of select block copolymers. The block copolymer dispersion stabilizers should have "anchor" blocks with coordinating groups for the cobalt surfaces, and "tail" blocks to extend into the reaction media (toluene in this case). Figures 2 and 3 illustrate cobalt nanoparticles generated in this manner utilizing the block copolymers discussed herein.

The copolymer chemical structures were designed such that the anchor blocks would crosslink tightly around the cobalt particles upon treatment at high temperatures (as opposed to having the polymer anchor blocks undergo chain scission with evolution of by-products). The polyvinylphenoxyphthalonitrile block formed a graphitic-like structure containing some nitrogen rings upon treatment at elevated temperatures (figure 4), while the polysiloxane anchor block formed a silica-like structure. An additional aspect that was important in designing these copolymers was to
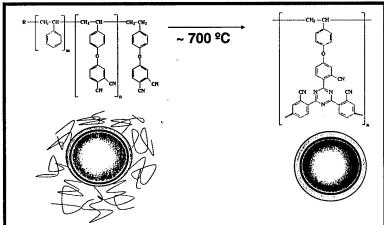
Figure 4. Poly(styrene-*b*-vinylphenoxyphthalonitrile) copolymers formed highly crosslinked networks upon heat treatment at 600-700 °C. During heat treatment, the styrene block degrades and the vinylphenoxyphthalonitrile block crosslinks to form a highly aromatic layer around the particle.

identify materials which yielded substantial residual char after the heat treatment to allow for protective coatings with reasonable thickness to form. For example, the residue for a poly(styrene-

b-vinylphenoxyphthalonitrile) block copolymer (top of figure 1) with 21 wt % poly(vinylphenoxyphthalonitrile) after heating at 700 °C was 26 wt %. Similar experiments also confirmed that poly(dimethylsiloxane-*b*-methyltrialkoxysilethylsiloxane) (bottom of figure 1) formed stable, shiny black residues with high char yields (figure 5). Thus, both copolymer structures were designed to yield highly crosslinked networks around the cobalt to serve as protective barriers against intrusion by oxygen.

Cobalt nanoparticles were prepared in toluene in the presence of each of these block copolymer types. The toluene was removed and these coated nanoparticles were subjected to pyrolyses in rigorously inert atmospheres at temperatures ranging from 300-700 °C. The resultant materials that had been heat-treated at 600-700 °C were brittle, black materials. Interestingly, the cobalt complexes encased in the graphitic-like coating were electrically conductive. X-ray photoelectron spectroscopy suggested that a silica-like coating formed around the cobalt for the cases of the particles originally encased in the polysiloxanes (figure 6).
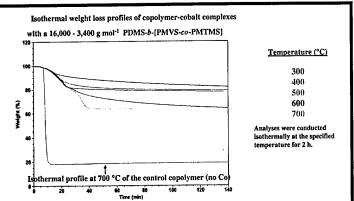

Figure 5. Isothermal weight loss profiles of cobalt -PDMS-b-[PMVS-co-PMTMS] copolymer complexes under nitrogen illustrate that about 60 weight percent of the complex is retained after treating it at 700 °C for 2 hours.

Transmission electron microscopy of the materials heated at 600-700 °C showed small cobalt particles that were adhered together. The approximately 10-nm diameter of the cobalt was at least predominantly retained (see figures 7 and 8 for examples). This is consistent with the work of others who have suggested that the sintering temperature of cobalt is about 900 °C. One cannot, however, discern from the photomicrographs whether any of the cobalt nanoparticles were "touching". The degrees of homogeneity of these coatings are also not yet clear.

The magnetic properties of the heat-treated materials were investigated with

Pyrolysis of Cobalt-Polymer Complexes at 700 °C Yields a Silica-like Surface

Annealing Temperature (°C)	Carbon (%)	Oxygen (%)	Silicon (%)	Cobalt (%)
Untreated	49	28	23	0
600	30	45	22	3
700	26	49	21	5

XPS Data for 16,000 – 3400 g mol⁻¹
PDMS-*b*-[PMVS-*co*-PMTMS] copolymer/cobalt complexes

Figure 6. Atomic compositions of the surfaces of cobalt-polysiloxane complexes after controlled heat treatments suggest that a silica -like surface forms.

vibrating sample magnetometry at room temperature (figures 9 and 10), and compared with the original cobalt complexes that were generated at 110 °C (toluene reflux). The magnetizations of the non-heat treated complexes ranged from 90-110 emu g⁻¹ of cobalt, and were consistent with those reported by others previously. During the heat treatments, portions of the organic polymers were lost via pyrolysis as the densified coatings formed. Thus, it was expected that the specific saturation magnetizations of these complexes would increase, and that the increases could at least be partially attributed to higher compositions of the metal. Surprisingly, however, at temperatures of approximately 200-500 °C, the saturation magnetization of the cobalt increased somewhat (in general, from about 100 to 120 emu g⁻¹ of cobalt). Moreover, after pyrolysis at 600-700 °C, the

magnetizations approached that of bulk cobalt (approximately 162 emu g^{-1}). This total process leads to coated cobalt nanoparticles with extremely high specific saturation magnetizations ranging from approximately 50-100 emu g^{-1} (for the complexes). The reasons for these differences in magnetic properties with specified heat treatments are as yet unclear.
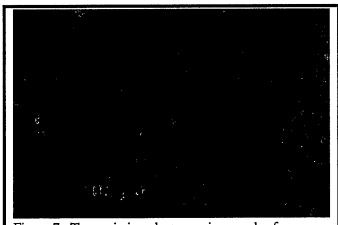
Figure 7. Transmission electron micrograph of a cobalt-poly(styrene-b-vinylphenoxyphthalonitrile) complex after treatment at 700 °C.

Cobalt Particle Size is Retained after Pyrolysis

MLV-600-16   100nm   WD = 4 mm   EHT = 5.00 kV   Signal A = InLens
                           Mag = 20.00 K X   Photo No. = 439   Date :12 Aug 2003

16,000 g mol^{-1} – 3400 g mol^{-1} PDMS-*b*-[PMVS-*co*-PMTMS] copolymer/cobalt complexes pyrolyzed at 600 °C
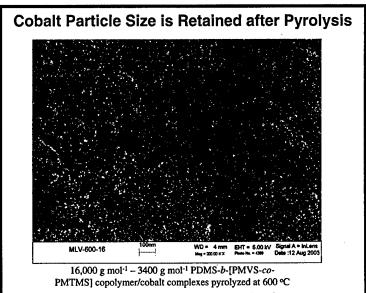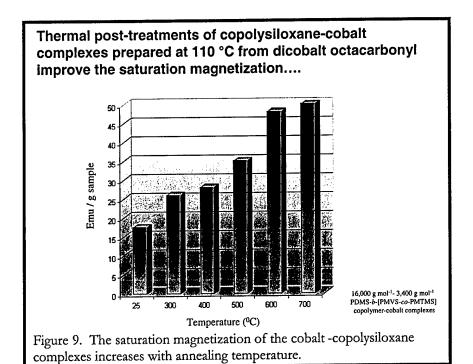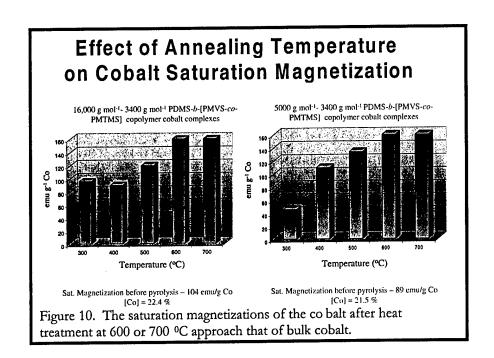
Figure 8. Transmission electron micrograph of a representative cobalt-polysiloxane complex after heat treatment at 600 °C for 2 hours.

Thermal post-treatments of copolysiloxane-cobalt complexes prepared at 110 °C from dicobalt octacarbonyl improve the saturation magnetization....

16,000 g mol⁻¹- 3,400 g mol⁻¹
PDMS-*b*-[PMVS-*co*-PMTMS]
copolymer-cobalt complexes

Figure 9. The saturation magnetization of the cobalt -copolysiloxane complexes increases with annealing temperature.

Effect of Annealing Temperature on Cobalt Saturation Magnetization

16,000 g mol⁻¹- 3400 g mol⁻¹ PDMS-*b*-[PMVS-*co*-PMTMS] copolymer cobalt complexes

5000 g mol⁻¹- 3400 g mol⁻¹ PDMS-*b*-[PMVS-*co*-PMTMS] copolymer cobalt complexes

Sat. Magnetization before pyrolysis – 104 emu/g Co
[Co] = 22.4 %

Sat. Magnetization before pyrolysis – 89 emu/g Co
[Co] = 21.5 %

Figure 10. The saturation magnetizations of the co balt after heat treatment at 600 or 700 °C approach that of bulk cobalt.

We have begun aging studies under ambient conditions of the cobalt nanoparticles coated with both the graphitic-like and silica-like coatings (figures 11 and 12), and the initial results are promising. Further critical durability investigations coupled with an understanding of the magnetic properties of these materials will be conducted collaboratively with our Australian collaborators over the next year.

Oxidation Study of Cobalt Nanoparticles Coated with Various Polymeric Materials

Saturation Magnetization (EMU / g)
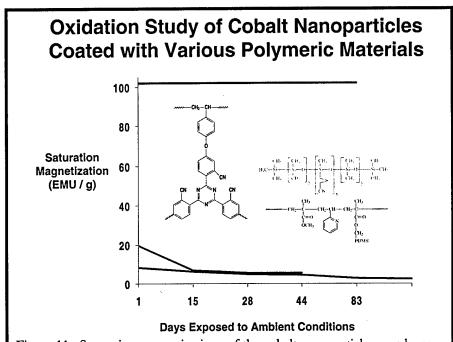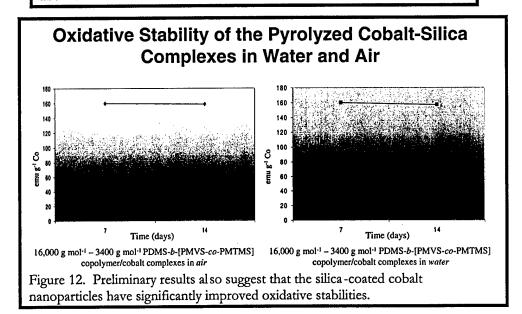
Days Exposed to Ambient Conditions

Figure 11. Saturation magnetizations of the cobalt nanoparticle complexes which were coated with the graphitic-like materials are stable in air and are higher than previously measured materials in our laboratories by a factor of about 5.

Oxidative Stability of the Pyrolyzed Cobalt-Silica Complexes in Water and Air

emu g^{-1} Co

Time (days)

16,000 g mol^{-1} – 3400 g mol^{-1} PDMS-*b*-[PMVS-*co*-PMTMS] copolymer/cobalt complexes in *air*

emu g^{-1} Co

Time (days)

16,000 g mol^{-1} – 3400 g mol^{-1} PDMS-*b*-[PMVS-*co*-PMTMS] copolymer/cobalt complexes in *water*

Figure 12. Preliminary results also suggest that the silica-coated cobalt nanoparticles have significantly improved oxidative stabilities.

In-Vitro Investigations of Cell Survival in the Presence of Magnetite-Copolymer Nanoparticle Complexes

Magnetite nanoparticles display strong ferrimagnetic behavior, and are less sensitive to oxidation than magnetic transition metal nanoparticles such as cobalt, iron, and nickel. For *in-vivo* applications, well-defined organic coatings are needed to surround the magnetite nanoparticles and prevent any aggregation. One goal of this segment of the research was to develop complexes of magnetite nanoparticles coated with well-defined hydrophilic polymers, so that they could be dispersed in aqueous fluids. Focal points have included: (1) Investigations of polymer systems which bind irreversibly to magnetite at the physiological pH, (2) The design of block copolymers with anchor and tail blocks to enable dispersion in biological fluids, and (3) Investigations of copolymer block lengths to maximize the concentration of bound magnetite.
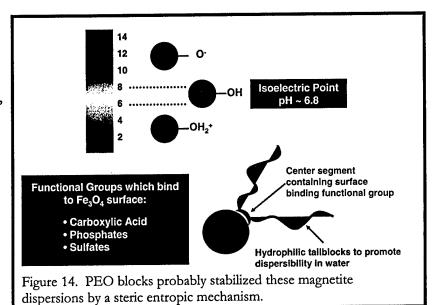
Hydrophilic triblock copolymers with controlled concentrations of pendent carboxylic acid binding groups were designed as steric stabilizers for the magnetite nanoparticles (figure 13). These

Figure 13. Hydrophilic block copolymer dispersion stabilizers for magnetite nanoparticles in water. The outer PEO tail blocks provide dispersion stability via steric repulsion, and the central polyurethane anchor block containing the carboxylic acid groups binds to the magnetite surfaces.

copolymers were comprised of controlled molecular weight poly(ethylene oxide) tail blocks and a central, polyurethane anchor block containing carboxylic acids. Stoichiometric aqueous solutions of $FeCl_2$ and $FeCl_3$ were condensed by reaction with NH_4OH to form magnetite nanoparticles, then a dichloromethane solution of the block copolymer was added to adsorb the copolymer onto the magnetite surfaces at pH 5. The isoelectric point of magnetite lies between 6 and 7. Thus, at pH 5, the central block of the copolymer contains carboxylate anions and the net charge on the magnetite surface is positive. Stable magnetite dispersions were prepared with all of the triblock copolymers. It was reasoned that the mechanism of adsorption was electrostatic, but that the PEO tail blocks stabilized the dispersions sterically (figure 14). Electrophoresis measurements in the growth media for the cell culture studies confirmed the absence of significant surface charge on the complexes.

The polymer-magnetite nanoparticle conjugates had a

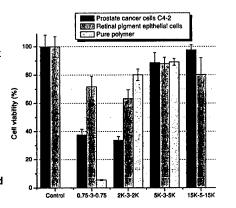Figure 14. PEO blocks probably stabilized these dispersions by a steric entropic mechanism.

maximum saturation magnetization of 34 emu g^{-1}, and magnetization curves showed minimal hysteresis. Powder X-ray diffraction, selected area electron diffraction and high resolution electron microscopy confirmed the magnetite crystal structure. Transmission electron microscopy showed that the dispersions contained magnetite particles coated with the polymers with a mean diameter of 8.8 ± S.D. 2.7 nm. The synthesis of these block copolymer stabilizers and the method for preparing the magnetite complexes has been published [7].

These magnetite-copolymer complexes were purified by repeated centrifugations to remove any magnetite that may not have been tightly encased in the copolymers, then by dialysis with Millipore water for a minimum of a week. MTT cell survival assays were conducted with each complex utilizing two cell lines: (1) Human prostate cancer cells (C4-2) and (2) Human retinal pigment epithelial cells. Cell proliferation and cell survival were compared to control populations (figure 15). A series of materials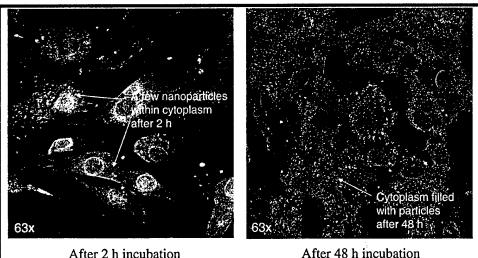 were studied wherein the average lengths of the PEO tail blocks were varied from 750 to 15,000 g mol^{-1}. Cell proliferation was found to be strongly dependent on the tail block length. It should be noted that the central polyurethane blocks of these materials are insoluble in water even though they contain carboxylic

Toxicity of magnetic nanoparticles seems to be dependent on PEO tail length:

• Low molecular weight PEO-coated magnetic nanoparticles (750 Da and 2 KDa) are quite cell toxic
• Higher molecular weight PEO-coated magnetic nanoparticles (5 KDa and 15 KDa) are not cell toxic
• **These results were confirmed by confocal microscopy studies**

Nanoparticle-polymer complex concentration 5 mg/mL; 7-35 wt % magnetite in the complexes

Figure 15. MTT assays with C4-2 human prostate cancer cells and human retinal pigment epithelial cells suggest that magnetite copolymer complexes with poly(ethylene oxide) block molecular weights of about 5000 g mol^{-1} and above are not cell toxic, while complexes with lower molecular weights blocks are toxic.

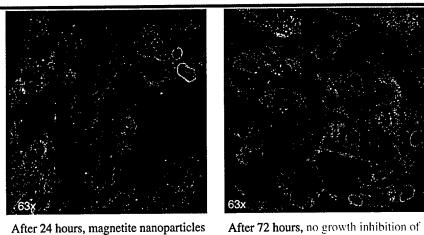After 2 h incubation   After 48 h incubation

with 2 K PEO - 3 COOH - 2 K PEO with 23 wt % of 8.7 nm diameter magnetite

Figure 16. Time course of uptake of magnetite-polymer complexes into human retinal pigment epithelial (HRPE) cells.

acids on each repeat unit, and this indicates that the central block has significant hydrophobic character. The weight fractions of the hydrophilic blocks in the four block copolymers described in the MTT assays in figure 15 are 0.55 (for the 0.75-3-0.75 copolymer), 0.77 (2k-3-2k), 0.89 (5k-3-5k) and 0.94 (15k-5-15k). Thus, the copolymers in the complexes which do not exhibit toxicity in the

MTT assays were significantly more hydrophilic relative to the materials which resulted in toxicity. Thus, the reasons for the differences in toxic responses of the more hydrophobic, lower molecular weight materials to this assay are not well understood as yet.

Confocal micrographs confirmed that all of the magnetite-hydrophilic polymer complexes were taken up into the cytoplasm of both cell lines (figures 16 and 17). Although the magnetite nanoparticles were only 8-9 nm in diameter, reflection optical micrographs clearly showed that they were taken up by the cells. For cases where the copolymer stabilizers had block lengths of 5000 g mol^{-1} and higher, both types of cells appeared to proliferate in a healthy manner.

After 24 hours, magnetite nanoparticles coated with 5 K PEO show up in "healthy," growing HRPE cells

After 72 hours, no growth inhibition of HRPE cells is visible; lots of nanoparticles have been incorporated

Figure 17. Confocal microscopy of HRPE cells in the presence of magnetite-polymer complexes suggest that the magnetite (bright spots) is taken up into the cytoplasm of the cells, but the cells appear to proliferate in a healthy manner.

Preparation of 100-500 nm Diameter Magnetite and Design of Biocompatible Polymer Coatings

This portion of the research has focused on preparing controlled-size magnetite nanoparticles (≤100 nm in diameter) and on the design of biocompatible polymer coatings for such particles. The goal has been to develop sub-micron magnetic particles with higher concentrations of the magnetic components. It is anticipated that particles approximately 100-nm in diameter should be sufficiently small to disperse via steric mechanisms in aqueous fluids, and that the metal oxide concentration of individual particles could be significantly higher than state of the art microsphere materials.

The approach has been to dissolve goethite crystals in glycol/water/acid media at 230-300 ^{0}C to reduce the goethite to magnetite, and crystallize magnetite crystals from these solutions under conditions of controlled nucleation and growth. It is well-known that carboxylic acids can complex with magnetite surfaces. Thus, an unsaturated dicarboxylic acid (e.g., itaconic acid) was added to the reducing solutions. Magnetite crystal size could be reduced from approximately 300 nm in diameter in ethylene glycol/water alone, whereas the size could be reduced to approximately 100 nm in diameter in the presence of controlled concentrations of itaconic acid (figure 18). Atomic compositions of the resultant surfaces were analyzed with X-ray photoelectron spectroscopy. The C_{1s} peaks in figure 18 display a strong high energy peak at 288.8 ev, signifying the presence of the itaconic acid carbonyl group at the surface.

Triblock copolymers containing poly(epsilon caprolactone) (PCL) endblocks and a central binding block containing multiple carboxylic acids were prepared to adsorb onto these 100-nm particles. These were synthesized by equilibrating 1,3,5,7-tetramethyl-1,3,5,7-tetravinylcyclotetrasiloxane with 1,3-bishydroxybutyltetramethyldisiloxane and an acid catalyst. The resultant polysiloxane hydroxylbutyl endgroups were utilized to initiate caprolactone and polymerize controlled molecular weight endblocks.

Goethite was reduced to magnetite in a solution of 1 g itaconic acid (1.5 x 10⁻² moles COOH), 60 mL ethylene glycol, and 10 mL water at 230 °C (under pressure) over 12 h.

XPS of approx. 100 nm magnetite particles coated with itaconic acid

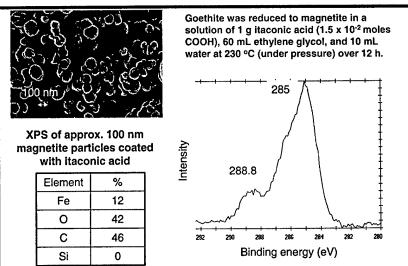| Element	%
Fe	12
O	42
C	46
Si	0

Figure 18. Goethite (FeOOH) was reduced to magnetite utilizing itaconic acid to bind with the magnetite and limit the crystal size. Magnetite nanoparticles approximately 100 nm in diameter form which are coated with itaconic acid.

Subsequently, mercaptoacetic acid was added across the pendent vinyl groups of the central block in free radical reactions to produce a polysiloxane anchor block. Our goal is to coat the 100-nm diameter magnetite particles with the polyester-*b*-siloxane block copolymers, then to investigate blends of those coated materials with high molecular weight poly(L-lactide) to form biodegradable microspheres. This segment of the research will be pursued over the next year in efforts to prepare magnetite-polylactide particles, then post-reactions of streptavidin onto the surfaces will be investigated (in collaboration with Kaminski and Rosengart at Argonne National Labs and the University of Chicago Medical School respectively).

Summary

Our research on the development and characterization of magnetic nanoparticle-polymer complexes over the past year has yielded approximately 10-nm diameter cobalt particles coated with both a graphitic-like and a silica-like coating. The small particle sizes appear to be retained after the protective coating is applied, but the particles are adhered together. The specific saturation magnetizations of the resultant particles range from 50-100 emu g⁻¹, which is up to about 5 times the response of our previous nanoparticle materials. Early durability results against oxidation are promising. Our research in this area over the next year will focus on breaking up the adhered materials, durability measurements, and on developing biocompatible coatings to redisperse these materials. Collaborations with Prof. St. Pierre's biophysics groups in Australia will be valuable to understand the magnetic properties of these new materials.

We have begun in-vitro tests to analyze magnetite nanoparticles coated with hydrophilic block copolymers. MTT assays for cell proliferation and survival utilizing human prostate cancer C4-2 cells and human retinal pigment epithelial cells suggest that avoiding toxicity may depend on the block lengths of the PEO tailblocks (which is concurrent with increased hydrophilicity of the copolymer stabilizers). Confocal microscopy indicates that these small polymer-magnetite complexes are taken up into the cytoplasm by both types of cells, irrespective of the stabilizer block

lengths. Relationships between chemical structure of the complexes and complex-cell interactions is an important issue, and we are pursuing related funding to continue this portion of the work in collaboration with Dr. Urs Hafeli at the Cleveland Clinic Foundation.

We have successfully prepared magnetite nanoparticles which are approximately 100-nm in diameter via controlled nucleation and growth processes in the presence of carboxylic acids. It is thought that the carboxylic acid probably binds to the magnetite surfaces during crystal growth and that this limits the crystal sizes. Our goal is now to coat these 100-nm magnetite particles with a biodegradable poly(L-lactide), then to subsequently functionalize the polylactide with streptavidin (via reaction of the pendent lysine groups on the protein with the polyester). This work is in collaboration with Drs. Kaminski and Rosengart (Argonne and the University of Chicago).

References:

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